Platform Biocatalysis and Biosynthesis

biotechnet
switzerland

History

Platform Biocatalysis and Biosynthesis

Dec. 2015

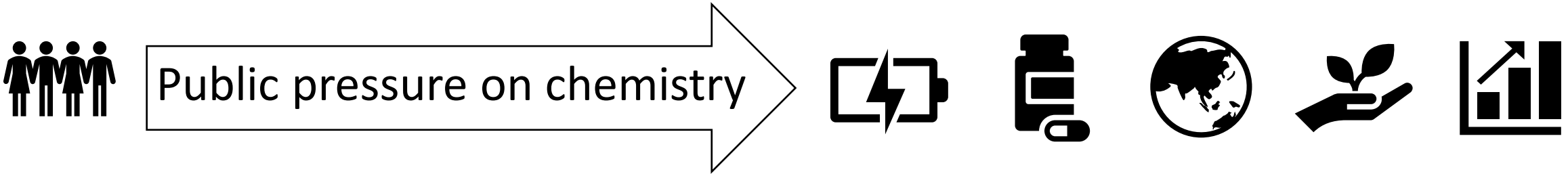
Jan. 2016

ZHAW – Wädenswil
Competence Center for Biocatalysis (CCBIO)

Prof. Dr. Rebecca Buller

Biocatalysis and Biosynthesis

"uses enzymes to catalyze reactions in synthetic chemistry"



Enzyme

high selectivity

ambient conditions

no rare metals

no protection groups

less organic solvents

use of non-fossil, renewable (waste) starting material

Bioinformatics
Machine learning
Molecular biology
Gene synthesis

enzymes can be modified to fit special applications

Chemist's Toolbox

Biocatalysis and Biosynthesis

Applications

- production of pharmaceutical blockbuster molecules/ drug discovery
- fine chemicals (aroma, fragrances, nutraceuticals) and
- commodity chemicals from sustainable resources

Future Applications

- novel compounds

Mission

- *Promote Biocatalysis and Biosynthesis* as a complementary method to chemical synthesis
- *Bundle relevant research competences* in Switzerland
- Help *bridge the gap* academic laboratories - the production plant
- Develop a comprehensive *biocatalytic toolbox*
  - enzyme libraries/ biocatalytic methods
- *Train* scientists to work in this interdisciplinary environment

→ Lowering barrier of acceptance for using biocatalysis and biosynthesis

Platform Members

Prof. Dr. Regine Eibl
Cell Culture Technology

Prof. Dr. Dieter Eibl
Biotechnology

Dr. Lukas Neutsch
Bioprocess Technology

Dr. Christin Peters
Biosystems Technology

Prof. Dr. Caspar Demuth
Analytical Technology

Prof. Dr. Martin Sievers
Micro- & Molecular Biology

Dr. Peter Riedlberger
Chemical Engineering

Prof. Dr. Achim Ecker
Industrial Chemistry

Prof. Dr. Rainer Riedl
Active Substance Research

Prof. Dr. Rebecca Buller
Biocatalysis

Biocatalysis Group at ZHAW

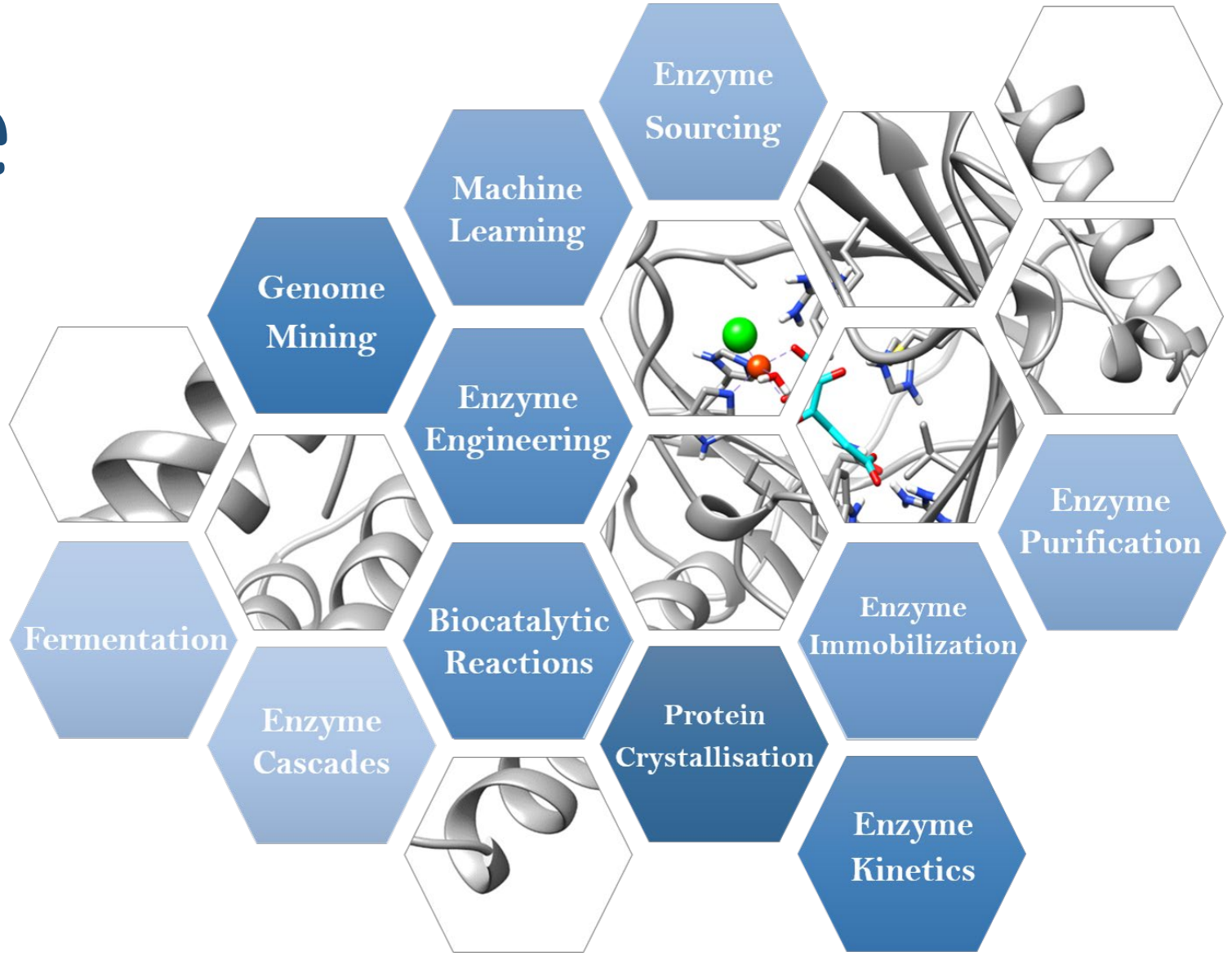
Head: Prof. Dr. Rebecca Buller

Research scientists

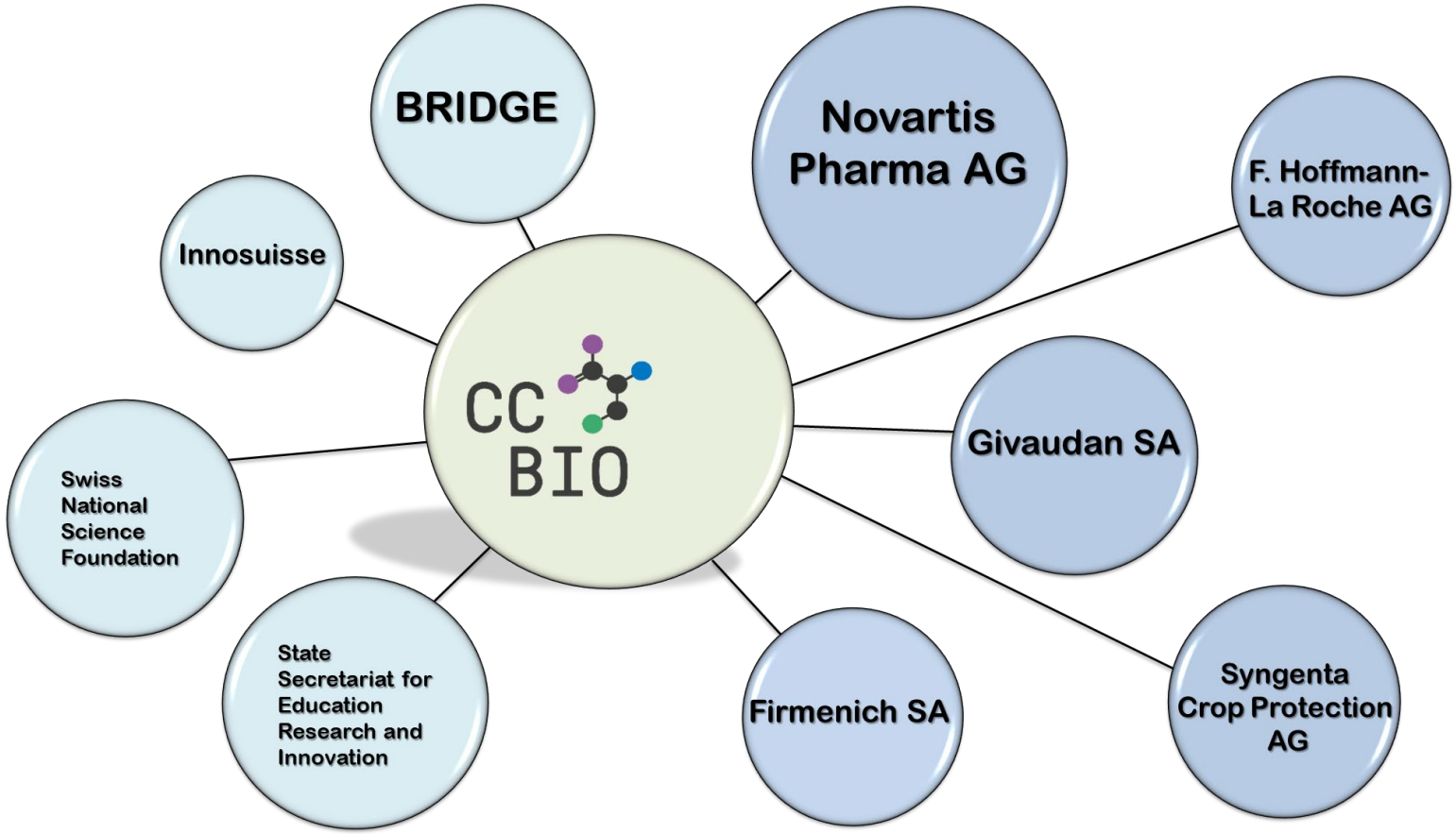
PhD students

Master and Bachelor students

Expertise


Enzyme Sourcing
Machine Learning
Genome Mining
Enzyme Engineering
Enzyme Purification
Fermentation
Biocatalytic Reactions
Enzyme Immobilization
Enzyme Cascades
Protein Crystallisation
Enzyme Kinetics

Funding and Collaborations

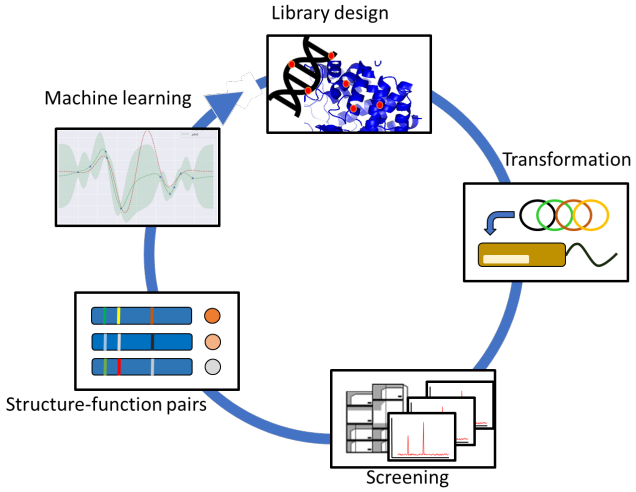


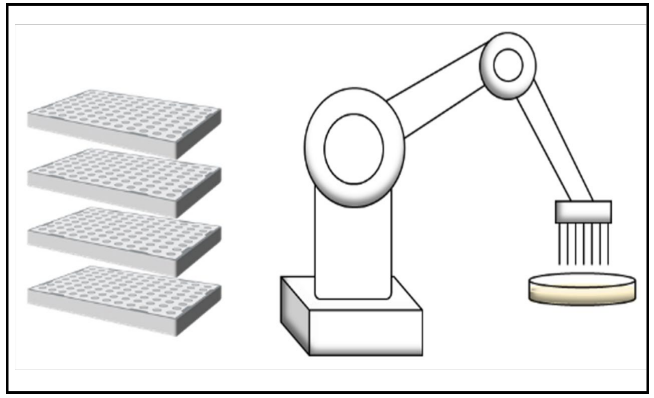
- Research projects
- Industrial Collaborations

Our Research Projects

Enzyme Families

- α-Ketoglutarate-dependent Oxygenases
- Halogenases
- Squalene-Hopene Cyclases
- Ene-Reductases
- Microbial Epimerases
- PETase



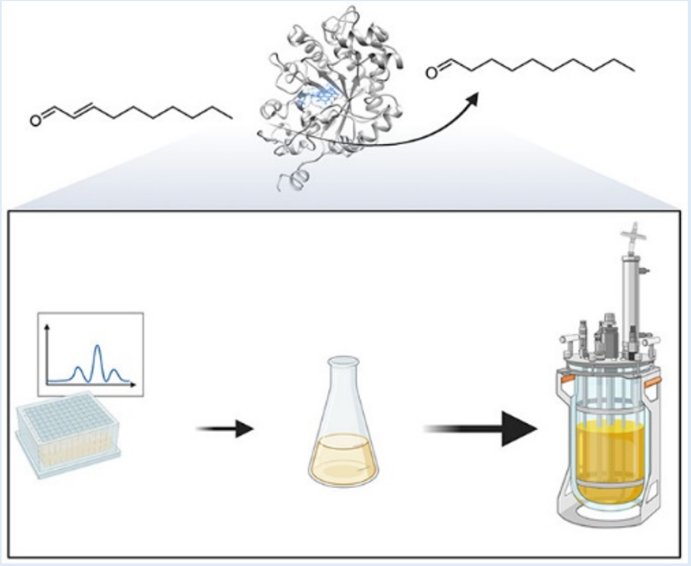


Technologies

- Algorithm-assisted enzyme engineering
- Automation-assisted enzyme engineering

2022 Publication

with platform member **Christin Peters** (ZHAW) and industrial partner **Firmenich**



Development of an Ene Reductase-Based Biocatalytic Process for the Production of Flavor Compounds

Org. Process Res. Dev, 2022.

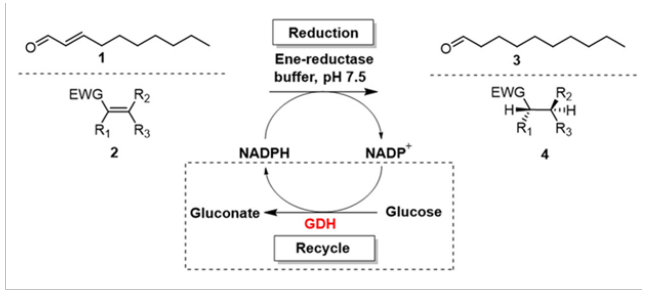
A. Papadopoulou, C. Peters, S. Borchert, K. Steiner, R. Buller.

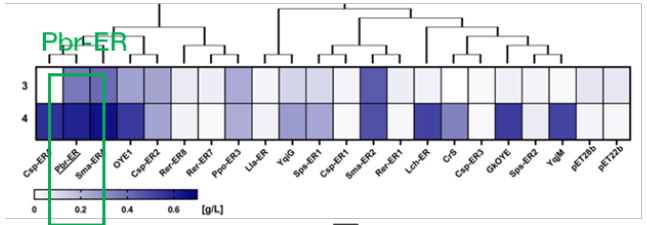
Co-funding: Innosuisse

2022 Publication

Development of an Ene Reductase-Based Bio-catalytic Process for the Production of Flavor Compounds

Org. Process Res. Dev. June 14, 2022





Pbr-ER

- WT-enzyme
- active pH 6.0-9.0
- processes up to 60g/L
- stable (-20°C, 14 months

- **Challenge**

  Find a biobased alternative to metal-or chemocatalyzed double bond reductions for the F&F industry

- **Method**

  Ene reductases catalyze reduction of activated alkenes → Screen a wild-type ene reductase library (20 enzymes)

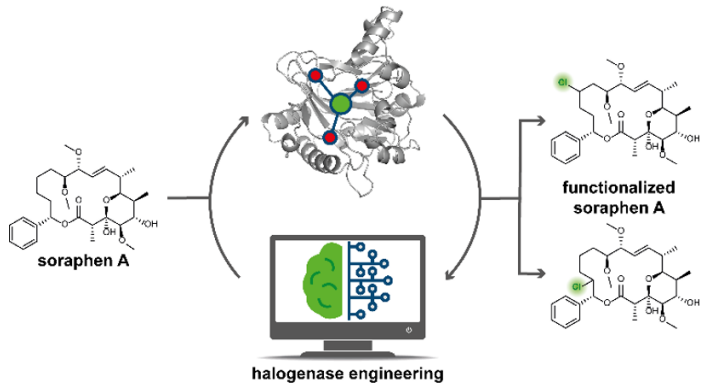
- **Results**

  Pbr-ER (*Pseudomonas brassicacearum*): 2*E*-decenal reduction (40g/L, 100mL scale), conversion >93% / 24h

  Active as well on undisclosed compound **2**

2022 Publication

with **Uwe Bornscheuer** (University of Greifswald) und industrial partner **Syngenta Crop Protection AG**



Algorithm-aided engineering of aliphatic halogenase WelO5* for the asymmetric late-stage functionalization of soraphens

Nat. Commun. 2022.

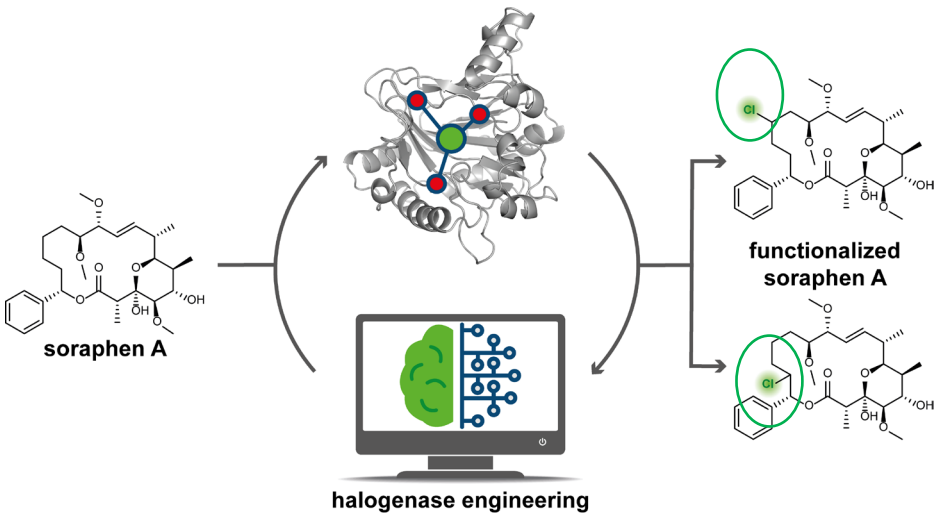
J. Büchler, S. Honda Malca, D. Patsch, M. Voss, N. J. Turner, U. T. Bornscheuer, O. Allemann, C. Le Chapelain, A. Lumbroso, O. Loiseleur and R. Buller

Co-funding SBFI-P-14 Innovation in Biocatalysis/ NCCR Catalysis

2022 Publication

Algorithm-aided engineering of aliphatic halogenase WelO5 for the asymmetric late-stage functionalization of soraphens*

Nature Communications. January 18, 2022



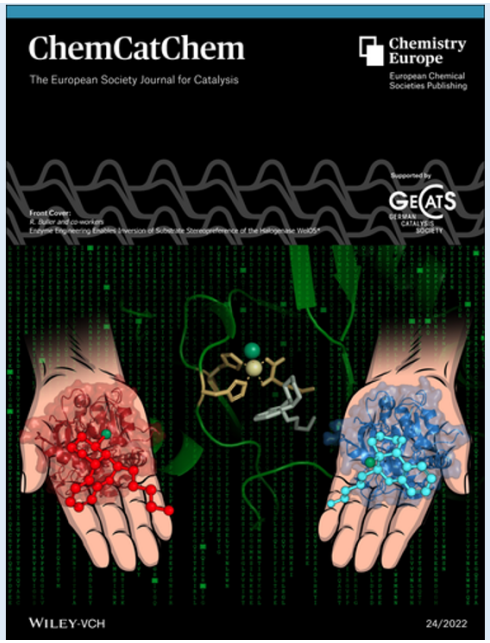
Biochemical characterization of selected WelO5* variants

Identification	WelO5* variant	app. k_{cat} [min^{-1}]	TTN
initial library	V81G_I161P	0.026 ± 0.007	0.30 ± 0.2
3-site combinatorial library	V81S_A88L_I161P	2.413 ± 0.349	30.0 ± 8.3
ML predicted	V81V_A88L_I161 A	1.959 ± 0.509	91.8 ± 22.0

- **Challenge**
  - Soraphen A is a potent natural antifungal - diversification
  - Find enzymes for controlled halogenation of sp^3 carbon
- **Method**
  - Build Soraphen A/ WelO5* model → use smart library design and machine learning → variants of halogenase WelO5* → chlorination activity
- **Results**
  - Smart library → enzymes accepting **polyketide** substrates
  - Machine learning → switch regioselectivity
  - Test on pathogen fungi → chlorinated compounds are active → starting point for further structure-function studies

2022 Publication

with industrial partner **Novartis** Institutes for BioMedical Research



Enzyme engineering enables inversion of substrate stereopreference of the halogenase WelO5*

ChemCatChem, 2022.

M. Voss, S. Hüppi, D. Schaub, T. Hayashi, M. Ligibel, E. Sager, K. Schroer, R. Snajdrova & R. M. U. Buller

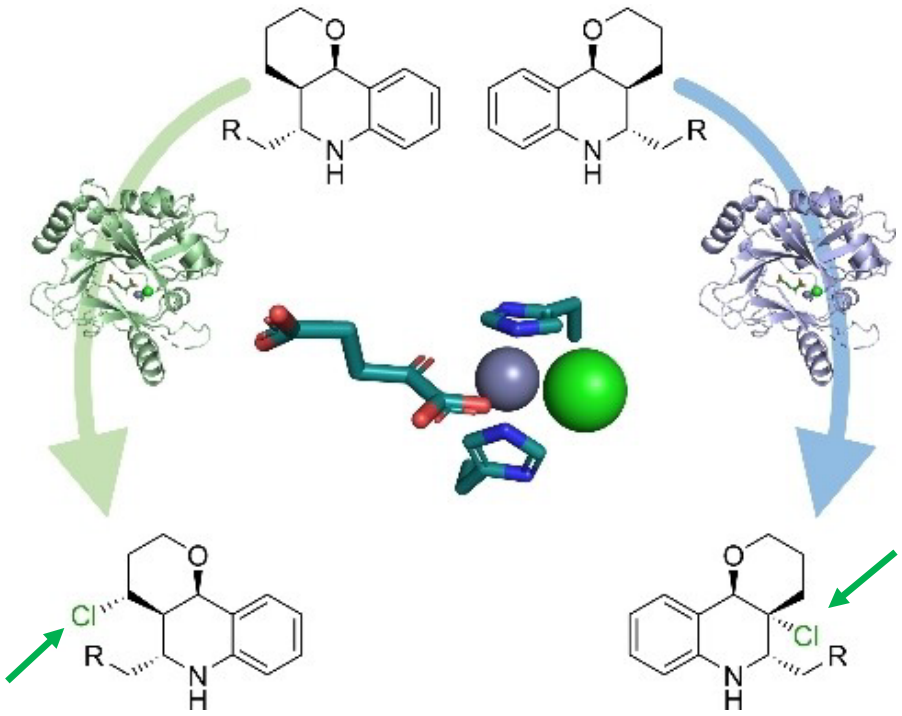
Co-funding SNF: NCCR Catalysis

Plattform Biocatalysis and Biosynthesis

2022 Publication

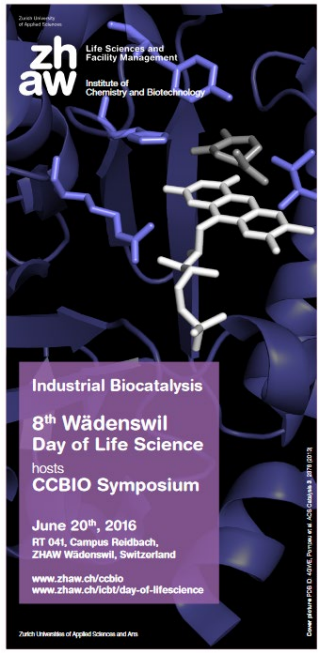
*Enzyme Engineering Enables Inversion of Substrate Stereopreference of the Halogenase WelO5**

ChemCatChem October 24, 2022

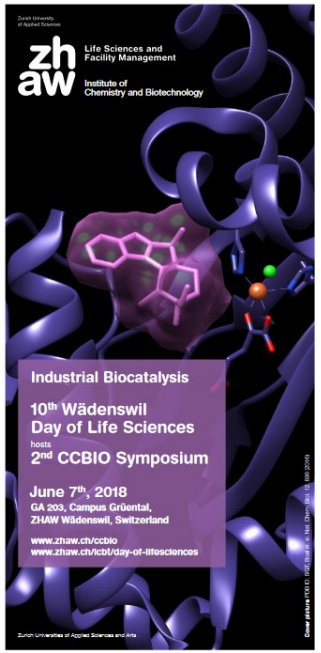


- **Challenge**
  - Regio- and stereoselective halogenation of sp^3 carbon
  - Racemic resolution of a mixture of stereoisomers generated during synthesis of a **martinelline-derived fragment**
- **Method**
  - 3-site combinatorial library → test on a martinelline-derived fragment isomers
- **Results**
  - Two enzyme variants identified → inverse stereopreference
  - Difference: three aa residues in active site
  - Selective halogenation of one isomer in a mixture

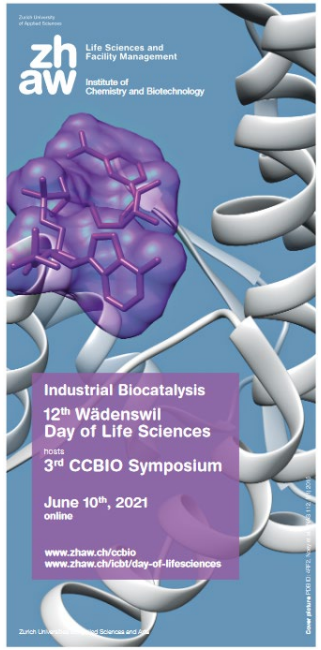
Conferences



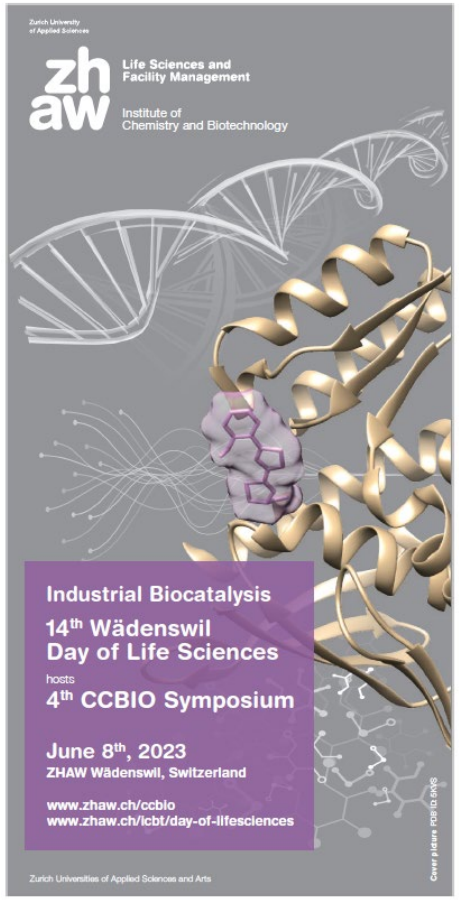
2016



2018



2021

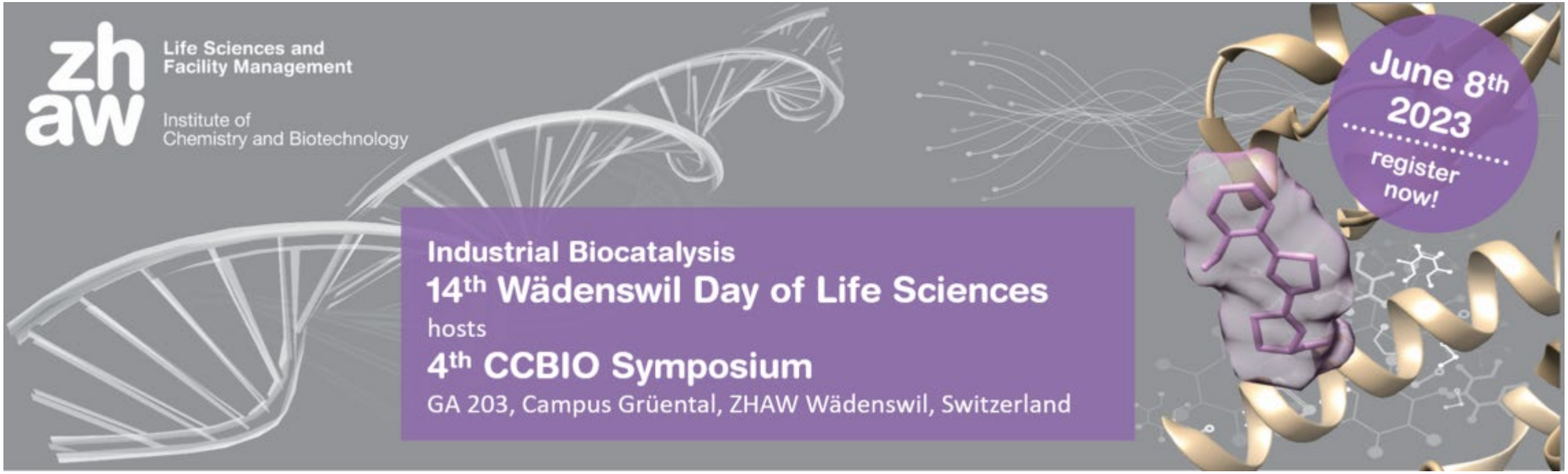


4th CCBIO Symposium "Industrial Biocatalysis"

June 8th, 2023

biotechnet switzerland

Plattform Biocatalysis and Biosynthesis



Confirmed speakers:

Sabine Flitsch, University of Manchester (UK)

Pablo Iván Nikel, Technical University of Denmark (DK)

Florian Rudroff, TU Wien (AT)

Mélanie Hall, University of Graz (AT)

Thierry Schlama, Novartis (CH)

Gerard Roelfes, University of Groningen (NL)

Jared Lewis, Indiana University Bloomington (US)

Xiongyi Huang, John Hopkins University Baltimore (US)

Jörg Pietruszka, Heinrich-Heine-Universität Düsseldorf (DE)

Caroline Paul, TU Delft (NL)

Christian Willrodt, BASF SE, Ludwigshafen (DE)

Plattform Biocatalysis and Biosynthesis

Join us:

Thursday June 8th, 2023

4th CCBIO Symposium "Industrial Biocatalysis"

www.zhaw.ch/ccbio

CC BIO

Competence Center for **Biocatalysis**

Connect with us:

rebecca.buller @zhaw.ch

www.zhaw.ch/ccbio

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